60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20160027A **DATE:** 12 June 2017

PROTOCOL TITLE: The Effect of Hypothermia on Prolonged Distal Aortic Balloon Occlusion in a Porcine Model (*Sus scrofa*) of Hemorrhage.

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Capt Meryl Simon Logan

DEPARTMENT: SGSE **PHONE #:** 707-423-7288

INITIAL APPROVAL DATE: 25 August 2016 **LAST TRIENNIAL REVISION DATE:** N/A

FUNDING SOURCE: SG

1. **RECORD OF ANIMAL USAGE:**

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	22	22	22

2. **PROTOCOL TYPE / CHARACTERISTICS:** (Check all applicable terms in **EACH** column)

___ Training: Live Animal	___ Medical Readiness	___ Prolonged Restraint
___ Training: non-Live Animal	___ Health Promotion	___ Multiple Survival Surgery
___ Research: Survival (chronic)	___ Prevention	___ Behavioral Study
_X_ Research: non-Survival (acute)	___ Utilization Mgt.	___ Adjuvant Use
___ Other ( )	___ Other (Treatment)	___ Biohazard

3. **PROTOCOL PAIN CATEGORY (USDA):** (Check applicable) ___ C _X_ D ___ E

4. **PROTOCOL STATUS:**

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

_X_ Completed, all approved procedures/animal uses have been completed

5. **Previous Amendments:**
List all amendments made to the protocol. **IF none occurred, state NONE. Do not use N/A.**

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change
1	10 Nov 16	Animal Use

6. **FUNDING STATUS:** Funding allocated: $25,725 Funds remaining: $0

7. **PROTOCOL PERSONNEL CHANGES:**

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? ___ Yes __X_ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

NAME	PROTOCOL FUNCTION	IACUC APPROVAL
N/A		

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

NAME	PROTOCOL FUNCTION	DATE OF DELETION
N/A		

8. **PROBLEMS / ADVERSE EVENTS:** Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None

9. **REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:**

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No

10. **PUBLICATIONS / PRESENTATIONS:** (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

Pending presentation of research at the fall 2017 AAST meeting, manuscript to follow

11. **PROTOCOL OBJECTIVES:** (Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?)

Yes. The hypothesis tested led to statistically significant results, leading us to pursue a phase II where ischemia and intervention times will be longer. If this continues to be successful, this can result in an easy to implement adjunct to prolonged REBOA and tourniquet use.

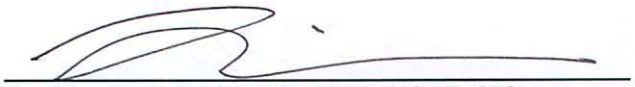
12. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objectives: We hypothesized that simple external cooling of the hind limbs would decrease ischemia-reperfusion injury following prolonged zone III REBOA.

Methods: 12 swine were anesthetized, instrumented, then underwent 15% blood volume hemorrhage. Animals were randomized to hypothermia or normothermia followed by 4 hours of zone III REBOA, resuscitation with shed blood, and 3 hours of critical care. Physiologic parameters were continuously recorded and laboratory specimens were obtained. Baseline and end-of-study muscle biopsies were obtained for histologic analysis.

Results: There were no significant differences between groups at baseline or after hemorrhage. No histologic differences were observed in hind limb skeletal muscle. Maximum creatine kinase was significantly lower in the hypothermia group compared to the normothermia group (median [IQR] = 3,445 U/mL [3,380-4,402] vs 22,544 U/mL [17,030-24,981]); $p < 0.01$). Maximum serum myoglobin was also significantly lower in the hypothermia group (1,792 ng/mL [1,250-3,668] vs 21,186 ng/mL [14,181-24,779]; $p < 0.01$). Fascial compartment pressures were significantly lower during critical care in the hypothermia group ($p = 0.03$).

Conclusion: External cooling during prolonged zone III REBOA decreased ischemic muscle injury and resulted in lower compartment pressures following reperfusion. Hypothermia may be a viable option to extend the tolerable duration of zone III occlusion. Future survival studies are required to assess functional outcomes.



MERYL SIMON-LOGAN, Capt, USAF, MC

20 JULY 17
(Date)

Attachments:
Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission **(Mandatory)**

Attachment 1

Defense Technical Information Center (DTIC) Abstract Submission

This abstract requires a brief (no more than 200 words) factual summary of the most significant information in the following format: Objectives, Methods, Results, and Conclusion.

Objectives: We hypothesized that simple external cooling of the hind limbs would decrease ischemia-reperfusion injury following prolonged zone III REBOA.

Methods: 12 swine were anesthetized, instrumented, then underwent 15% blood volume hemorrhage. Animals were randomized to hypothermia or normothermia followed by 4 hours of zone III REBOA, resuscitation with shed blood, and 3 hours of critical care. Physiologic parameters were continuously recorded and laboratory specimens were obtained. Baseline and end-of-study muscle biopsies were obtained for histologic analysis.

Results: There were no significant differences between groups at baseline or after hemorrhage. No histologic differences were observed in hind limb skeletal muscle. Maximum creatine kinase was significantly lower in the hypothermia group compared to the normothermia group (median [IQR] = 3,445 U/mL [3,380-4,402] vs 22,544 U/mL [17,030-24,981]); $p < 0.01$). Maximum serum myoglobin was also significantly lower in the hypothermia group (1,792 ng/mL [1,250-3,668] vs 21,186 ng/mL [14,181-24,779]; $p < 0.01$). Fascial compartment pressures were significantly lower during critical care in the hypothermia group ($p = 0.03$).

Conclusion: External cooling during prolonged zone III REBOA decreased ischemic muscle injury and resulted in lower compartment pressures following reperfusion. Hypothermia may be a viable option to extend the tolerable duration of zone III occlusion. Future survival studies are required to assess functional outcomes.

Grant Number:_____

From:_____

****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**